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The relationship between hemoglobin to red cell distribution width (RDW) ratio (HRR) and prognosis in patients with acute coronary syndrome

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ABSTRACT

Aims: The use of hematological parameters in the prognostic assessment of acute coronary syndrome (ACS) has become common in recent years. Thus, our study aimed to evaluate the relationship between hemoglobin to red cell distribution width (RDW) ratio (HRR) and prognosis of these patients.

Methods: A retrospective evaluation was conducted on patients who presented to the emergency department between 01.09.2023 and 01.04.2024 and received a diagnosis of ACS. HRR was determined by dividing the hemoglobin concentration by the red cell distribution width (RDW). The patients were categorized into two groups based on their HRR values: high HRR patients and low HRR patients, using a specified HRR cut-off value. Statistical comparisons were conducted on all parameters between the two patient groups. The variables potentially linked to mortality were analyzed using receiver operating characteristic (ROC) analysis.

Results: The in-hospital mortality rate, vasopressor needs, and MV support requirements were significantly higher in the low HRR (≤0.828) group than in the high HRR (>0.828) group ($p<0.05$ for all). The ROC analysis revealed that the HRR cut-off value for predicting mortality was 0.828. The sensitivity was determined to be 78.8% and the specificity was 92.5% (AUC: 0.885, $p<0.001$).

Conclusion: In patients with ACS, HRR measured at admission is a marker with a high prognostic value.

Keywords: Hemoglobin/red cell distribution width, acute coronary syndrome, prognosis, mortality

INTRODUCTION

Coronary artery disease (CAD), one of the most common causes of morbidity and mortality, endangers human health.[1] Acute coronary syndrome (ACS) is the prevailing type of CAD characterized by acute myocardial ischemia (AMI).[2] ACS encompasses a range of pathologies affecting the coronary arteries, including unstable angina (USAP), non-ST-segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI).[3] Major adverse cardiovascular events (MACE) are common in these patients, despite technological advancements like percutaneous coronary intervention (PCI). Hence, it is crucial to uncover suitable biomarkers that may be utilized for risk classification and enhance the prognosis of these patients.[4] Hematological markers have been increasingly essential in the prognostic assessment of ACS due to their comprehensive advantages, in recent years.[5]

Atherosclerosis is an inflammatory disease that significantly contributes to the development of cardiovascular disease (CVD). It is widely recognized that the prognosis of ACS is influenced by inflammatory markers.[6] The red cell distribution width (RDW) is a hematological parameter that indicates the size heterogeneity of red blood cells. Moreover, there is substantiated data indicating that RDW, which serves as an indicator of systemic inflammation, can accurately forecast an unfavorable prognosis in ACS.[7] Hemoglobin is another hematological parameter that serves as both a diagnostic and prognostic indicator of inflammatory diseases.[3] Leonardi S et al.[8] demonstrated that low hemoglobin levels are common in invasively treated ACS patients and increase 1-year mortality.In recent years, the hemoglobin/RDW ratio (HRR), calculated by dividing hemoglobin by RDW, has been shown to be a significant prognostic indicator in inflammatory disorders such stroke and sepsis.[9,10] However, few studies have

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been reported in the literature that investigate the association between HRR and patient outcomes in CAD.[1,2,11] Therefore, in our study, the link between HRR and prognosis in patients with ACS was examined.

METHODS

Study design and patient population

The study was carried out with the permission of the Faculty of Medicine, Necmettin Erbakan University Clinical Researches Ethics Committee (Date: 07.06.2024, Decision No: 5024-19823). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

A retrospective evaluation was conducted on patients who applied to the emergency department (ED) of a training and research hospital between 01.09.2023 and 01.04.2024. These patients were diagnosed with ACS based on their complaints, medical history, electrocardiography (ECG), and laboratory examinations. Additionally, they underwent coronary angiography (CAG). Patients over 18 years of age, male or female, whose all clinical and laboratory information could be accessed from the hospital registry system and whose diagnosis of ACS was confirmed according to current guidelines, were included in the study.[12]

The severity of the lesion in patients with USAP/NSTEMI was determined by calculating the thrombolysis in myocardial infarction (TIMI) and history, ECG, age, risk factors, and troponin (HEART) scores at the time of admission to the ED. Additionally, the SYNTAX risk scores were calculated for all patients after CAG.[13-15] Upon admission to the ED, the following information was collected from patients: age, gender, medical history, routine blood tests, type of ACS (including STEMI, NSTEMI, USAP), the need for vasopressor support and/or mechanical ventilation (MV) in the intensive care unit (ICU), length of stay in the ICU (LOS-ICU), length of hospital stay (LOHS), and outcomes (discharge or death). This data was obtained through the hospital registry system.

The evaluation of mortality was determined by the occurrence of death during hospitalization. The study excluded patients who were under 18 years old, receiving acute thrombolytic therapy, pregnant, had a history of acute/chronic hematological disease, cancer, active infection, immunosuppressed, or had inaccessible information in the electronic record system. The calculation of HRR involves dividing the hemoglobin concentration (g/dl) obtained from hemogram analysis by the RDW-CV (coefficient of variation) (%). The patients were categorized into two groups based on their HRR values: high HRR and low HRR, using a specified HRR cut-off value. Statistical comparisons were made between all parameters in these two patient groups. The variables potentially linked to mortality underwent receiver operating characteristic (ROC) analysis. In addition, the correlation between hemoglobin, RDW-CV, and HRR levels with TIMI, HEART, and SYNTAX risk scores was also assessed.

Hematological and Biochemical Analysis

During admission to the ED, blood samples were obtained to test RDW, hemoglobin, and Troponin I level. The hematological markers were assessed using the Mindray auto hematology analyzer BC-6800 device (Shenzhen, China). The biochemical parameters were measured using the Mindray chemistry analyzer BS-2000M device, (Shenzhen, China).

Statistical Analysis

Statical analysis in the study was performed using SPSS 27.0 (IBM Inc, Chicago, IL, USA) program. Kolmogrov-Smirnov test, histogram analysis, skewness/kurtosis data and Q-Q plots were used to evaluate the assumptions of normal distribution. Qualitative parameters were expressed as frequency and percentage (%). Descriptive statistics of scale data were expressed as IQR (median minimum - maximum) or mean±standart deviation according to distribution pattern. Relationships between the two groups are evalutated with independent t test or Mann-Whitney U test. Relationships between nominal parameters were detailed with either Chi-Square analysis or Fisher's exact tests. ROC analysis was performed to reveal the predictive values. In the entire study, the type-I error rate was taken as 5% (α=0.05) and $p<0.05$ was accepted as the significant limit.

RESULTS

Table 1 demonstrates the characteristics of the patients based on their HRR groupings. Out of the 245 patients, 42 had a low HRR group (≤0.828), whereas 203 had a high HRR group (>0.828). When comparing the high and low HRR groups based on gender, STEMI, NSTEMI, USAP, SYNTAX score, LOHS, and LOS-ICU, no significant difference was found ($p>0.05$ for all). In the low HRR group, several factors were found to have significantly higher values compared to other group. These factors include age, RDW, troponin I levels, TIMI score, HEART score, the need for vasopressor and MV support, and the in-hospital mortality rate ($p<0.05$ for all). In addition, the low HRR group exhibited significantly lower hemoglobin levels ($p<0.001$).

The ROC analysis of parameters in mortality prediction is presented in Table 2. Of all the parameters, the SYNTAX score did not show a statistically significant difference ($p>0.05$). Hemoglobin and HRR had exceptional predictive value among the blood parameters, (AUC:0.903, 0.885, respectively). Among the risk scores, the TIMI score had the highest AUC value, while the HEART score had the lowest AUC value (AUC: 0.775, 0.688, respectively).

The correlation between parameters is presented in Table 3. RDW had a significant positive correlation with both TIMI and HEART risk scores. A significant negative correlation was seen between hemoglobin levels and Troponin I, TIMI, and HEART risk scores. A significant negative correlation was identified between HRR and Troponin I, TIMI, and HEART risk score ($p<0.05$ for all).

Table 1. Characteristics of patients according to HRR groups

Variables	Low group (HRR ≤ 0.828) (n=42, %17.1)	High group (HRR >0.828) (n=203, %82.9)	p
Age, years	65.0±10.0	61.0±11.0	0.014
Gender			
Male, n(%)	28 (66.7%)	147 (72.4%)	0.453
Female, n(%)	14 (33.3%)	56 (27.6%)	
Laboratory parameters			
RDW-CV, (%)	16.6 (13.2-18.4)	13.4 (9.5-17)	<0.001
Hemoglobin (g/dl)	11.5 (8.5-13.6)	14.7 (11.3-17.7)	<0.001
Troponin I	1284.0 (4.0-21200)	178.0 (2.0-25000)	0.002
Diagnosis			
STEMI	10 (23.8%)	46 (22.7%)	0.223
NSTEMI	26 (61.9%)	103 (50.7%)	
USAP	6 (14.3%)	54 (26.6%)	
Scores			
TIMI	5 (2-7)	4 (2-7)	<0.001
HEART	8 (0-10)	7 (0-10)	0.035
SYNTAX	16 (3-39)	15 (1-50.5)	0.310
MV support, n (%)			
No	25 (59.5%)	193 (95.1%)	<0.001
Yes	17 (40.5%)	10 (4.9%)	
Vasopressor support			
No	19 (45.2%)	195 (96.1%)	<0.001
Yes	23 (54.8%)	8 (3.9%)	
LOHS, day	3 (0-5)	3 (2-8)	0.255
LOS-ICU, day	1 (1-5)	1 (1-3)	0.176
In-hospital mortality			
No	16 (38.1%)	196 (96.6%)	<0.001
Yes	26 (61.9%)	7 (3.4%)	

HRR: Hemoglobin to red blood cell distribution width ratio, RDW: Red blood cell distribution width, STEMI: ST-segment elevation myocardial infarction, USAP: Unstable angina pectoris, TIMI: Thrombolysis in myocardial infarction, HEART: History, electrocardiogram, age, risk factors, and troponin, MV: Mechanical ventilation, LOHS: Length of hospital stay, LOS-ICU: length of stay in the ICU.

Table 2. ROC analysis of parameters in mortality prediction

	AUC	95% CI		Cut-off	Sensitivity (%)	Specificity (%)	p
		Lower limit		Upper limit			
RDW	0.797	0.691	0.902	14.85	72.7%	85.8%	<0.001
Hemoglobin*	0.903	0.828	0.979	12.4	81.8%	93.4%	<0.001
Troponin I	0.787	0.717	0.856	842.0	84.8%	73.6%	<0.001
HRR*	0.885	0.798	0.973	0.828	78.8%	92.5%	<0.001
TIMI	0.775	0.688	0.862	≥4.5	81.8%	59.4%	<0.001
HEART	0.688	0.650	0.817	≥8.5	69.7%	74.5%	0.004
SYNTAX	0.601	0.488	0.714	≥17.7	60.6%	60.4%	0.080

ROC: Receiver operating characteristic, AUC: Area under the curve, CI: Confidence interval.
*Lower values are associated with positive (exitus) results.
HRR: Hemoglobin to red blood cell distribution width ratio, RDW: Red blood cell distribution width, TIMI: Thrombolysis in myocardial infarction, HEART: History, electrocardiogram, age, risk factors, and Troponin.

Table 3. Correlation relationship between parameters

		Troponin I	TIMI	HEART	SYNTAX	LOHS	LOS-ICU
RDW	rho (ρ)	0.111	0.167	0.153	0.098	0.023	0.016
	p	0.083	0.009	0.017	0.125	0.719	0.797
HBG	rho (ρ)	-0.165	-0.263	-0.145	-0.06	-0.049	-0.061
	p	0.01	<0.001	0.023	0.348	0.441	0.345
HRR	rho (ρ)	-0.135	-0.215	-0.154	-0.075	-0.029	-0.048
	p	0.035	0.001	0.016	0.240	0.652	0.456

HRR: Hemoglobin to red blood cell distribution width ratio, RDW: Red blood cell distribution width,HBG: Hemoglobin, TIMI: Thrombolysis in myocardial infarction, HEART: History, Electrocardiogram, age, risk factors, and troponin, LOHS: Length of hospital stay, LOS-ICU: Length of stay in the ICU.

DISCUSSION

Currently, it is recognized that systemic inflammation plays a significant role in the development and progression of CVD, regardless of traditional risk factors.[3] Multiple studies have demonstrated the significant predictive value of hematological parameters in patients with CAD. RDW is a hematological marker that is associated with inflammatory diseases and is an indicator of anisocytosis.[2] While the exact process remains uncertain, it is believed that RDW levels rise due to uncontrolled inflammation in patients with ACS.[1] Currently, there is evidence showing a significant relationship between elevated RDW values and the prognosis of CVD.[7,16] In a study conducted by Khaki et al.,[17] they found that patients with high RDW had a greater 6-month death rate compared to patients with low RDW, as shown in their analysis of 649 patients with ACS. According to Wei et al,[18] in a study involving 2078 patients with chest pain, the RDW cut-off value was determined to be 13.25%. This value was found to have a sensitivity of 78.10%, specificity of 87.44%, and an AUC of 0.88 in predicting myocardial damage. Additionally, RDW was found to be associated with hs-cTnT (r=0.607). Our study found a significant correlation between RDW and TIMI and HEART risk scores. Additionally, RDW predicted mortality with 72.7% sensitivity, 85.8% specificity, and an AUC value of 0.797. Consequently, RDW may serve as a prognostic marker in patients with ACS.

Hemoglobin levels, which indicate the capacity of the body to carry oxygen, serve as a significant marker of inflammation in patients with CAD.[3] Anemia, a frequently occurring condition caused by chronic inflammation, has been demonstrated to be linked with increased cardiac load, left ventricular hypertrophy, and CVD.[19] Acute anemia can disturb the natural balance of myocardial oxygen requirement, potentially leading to the development of AMI.[20] The study conducted by Ndrepepa et al.[21] examined 3838 patients with ACS and found that a reduction in hemoglobin levels during hospitalization was linked to an increased risk of mortality within one year, even in cases where there was no major bleeding. In their study, Kılıç et al.[2] examined 1.146 patients with ACS and found that the hemoglobin level was significantly lower in mortality group. Our study found a significant correlation between hemoglobin levels and Troponin I, TIMI, and HEART risk scores. Hemoglobin also demonstrated remarkable predictive ability for mortality in these patients (AUC: 0.903, sensitivity: 81.8%, specificity: 93.4%). While numerous studies have demonstrated the significance of RDW and hemoglobin levels in AMI, the prognostic value of HRR in this specific patient group remains uncertain.[2] By combining the data from hemoglobin and RDW into a single variable, HRR can be utilized as a more potent prognostic marker. Furthermore, considering that hemoglobin and RDW can be influenced by several factors such as nutrition, infection, etc., and so on, it is believed that HRR can mitigate these negative effects.[11] Several studies have established a significant relationship between HRR and the likelihood of survival among individuals diagnosed with cancer.[22,23] A study involving 1816 patients with heart failure demonstrated that HRR exhibited a non-linear relationship with 3-month hospital readmission.[24] Kılıç et al.[1] shown that HRR is a predictive value for MACE in the long-term follow-up after AMI. Xiu et al.[2] demonstrated that among patients with CAD who had low HRR levels (HRR<10.25), the long-term mortality rate following PCI was 1.470 times higher. In the study conducted by Huo et al.[4] with 4651 patients who underwent PCI, it was observed that the HRR was significantly lower in the group of patients

who died compared to those who survived. The findings of our study were in line with the aforementioned studies. Patients with low HRR were found to have a significantly higher need for vasopressor, MV support, and in-hospital death rate. ROC analysis revealed that the predictive power of HRR for mortality was found to be significantly high. Furthermore, since HRR has a significant correlation with Troponin I, TIMI, and HEART risk scores, HRR can also be employed as a valuable marker in the risk classification for these patients. However, no significant correlation was observed between HRR and the LOHS or LOS-ICU. This may be attributed to the characteristics of the patient population under study.

Limitations

We have a few limitations. First, due to the study's single-center and retrospective nature, it is not possible to rule out potential factors that may have influenced our findings. Secondly, only blood parameters at the time of admission were investigated, dynamic measurements of these parameters were not feasible. Third, due to the evaluation of short-term mortality and the limited sample size, the findings of our study cannot be extrapolated to a broader population. In order to validate our study findings, it is necessary to conduct larger-scale, multicenter studies including a significant number of participants.

CONCLUSION

Our study indicates that the levels of HRR evaluated upon admission are an employable marker that determines the prognosis of individuals with ACS. HRR can assist doctors in the risk classification of patients by virtue of its significant correlation with troponin I, TIMI, and HEART risk scores.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Faculty of Medicine, Necmettin Erbakan University Clinical Researches Ethics Committee(Date: 07.06.2024, Decision No: 5024/19823).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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